Ecological Health Risk of Joint Effect of Biological and Chemical Environmental Factors

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Abstract

The objective of this paper is to study common mechanisms and patterns of joint effect of biological and chemical factors on the human body starting from experiments on animals. The subchronic experimental study was performed on 700 guinea pigs (inhalation with sulphur dioxide and AD). Aspects of risk evaluation isolated and joint with chemical factor biotechnological products presented as microorganisms-producers of feed additives and a final albuminiferous product are considered in this study. It was showed that application of AD and sulfur dioxide develops a response in the form of sensitization, allergopathy and toxico-allergopathy characteristics and patterns of pig's organism response to exposure of products of biotechnological synthesis have been determined.

Keywords

Joint Effect; Chemical and Biological Fctors; Sulphur Dioxide; AD; SDT; HDT

Introduction

The development of the biotechnological industry yields opportunities to solve the problems of material and food resources, environmental pollution, energy supply, and public health care, as well as to meet the demands of humanity, in addition, it also opens possibilities to produce new kinds of goods. Modern production technologies include biotechnological methods used in manufacture of feed additives, hydrolytic yeast, interferon, enzymes, antibiotics, amino acids, plant protection products, farming multi-enzyme systems, insulin, and other bioactive substances. Manufacture of these products involves similar hygienic parameters determined by the biological nature of materials used in the production process and of the final products. Biotechnological advances can be limited by possibility of a biological environmental pollution resulted from the way that these new products are obtained. Some studies have addressed strategies to solve the toxic-hygienic and ecological problems caused by biological pollution as opposed to well studied chemical pollution. Moreover, the isolated exposure effects of the introduction of a biological factor are considered by many to be an uncommon event (N. I. Sheina, 2011).

There are no approved criteria used to evaluate the joint effects of biological and chemical factors. The data presented herein is derived from long-term studies performed at the Eastern Siberian Scientific Center of Human Ecology of the Siberian Branch of the Russian Academy of Medical Sciences (ESSHE SB RAMS) that concern theoretical and practical aspects of ecological risk evaluation of the joint effects of a biological agent, the dust of an albuminiferous product manufactured using a microbiological synthesis of yeast-like fungi Candida, and a chemical sulfur dioxide.

The initial study was triggered by an event in Angarsk city in October 1988for patient complaints on bronchospasm which drew the attention of Angarsk city emergency medical departments (L. M. Sosedova, 2003). The Angarskiy biotechnological plant having operated for 10 years released an albuminiferous dust (AD), a by-product of the microbial synthesis, into the air of the surrounding residential area. Quantities of AD released into the air were higher than the maximum permissible amounts. In October 1988, there was no wind during a 7-day period and, consequently, there was no dispersion of pollutants accumulating in the air. Different commissions investigating the source of the patient's illnesses failed to reach a conclusion. They reported that either AD or a chemical factor (sulfur dioxide) was the main cause of the patient's

illnesses. Sulfur compounds such as sulfur dioxide were the most common air pollutants which was known that during that period the concentration of sulfur dioxide in the air had dramatically increased.(2-4 mg/m3) (L. M. Sosedova, 2003).

Materials and Methods

An experimental study was performed on 700 guinea pigs provided by General Scientific Center VB "Vector" (Novosibirsk, Russia) in which each group included 8–12 mature laboratory animals. The experiments on animals were performed according to the European Convention for the Protection of Vertebrate Animals Used for Experimental and other Scientific Purposes (ETS 123) Strasbourg, 1986. The studies were carried out in accordance with the approved protocol by the Bio-ethical Committee of ESSHE SB RAMS, standard study operational procedures, and sanitary guidelines for settings, equipment, and maintenance of experimental biological clinics (vivaria). Sterile sawdust was used as bedding for all animals. Standard combined granular complete diet feeding (extruded) for laboratory animals was used for small laboratory animals. Unlimited treated tap water was provided in standard drinkers for all animals. The animals were kept in controlled environmental conditions with air temperature of 18-22°C and a relative humidity of 60-70%. Setting lighting was natural-artificial. Newly arrived animals were placed in cages in quarantine for 7 days.

Microbiological products of biotechnological synthesis are known to be albuminiferous allergens, which can cause not only hypersensitivity (sensitization) but also small-dose (SDT) or high-dose (HDT) tolerance. Therefore, three baseline models under AD exposure were examined: sensitization, SDT and HDT. Sensitization of guinea pigs was achieved by injection of 500 μg AD mixed with incomplete Freund's adjuvant under the hind limb aponeurosis. To induce tolerance, a 150 μg (SDT) or a 5000 μg (HDT) water-soluble AD polysaccharide antigen was injected intracardially into experimental animals under light ether anesthesia for 14 days before sensitization. Inhalation priming with sulfur dioxide was performed by placing guinea pigs in prime chambers for 4 hours per day for each in the period of 10 days. The sulfur dioxide concentration (2-4 mg/m3), temperature, and humidity were maintained at the same level. Sulfur dioxide inhalation was performed on three occasions: 14 days before AD injection, simultaneousness with AD injection, and 14 days after AD injection.

The animals were tested for hypersensitivity 21-28 days post priming termination. Instant and delayed-type hypersensitivity were determined by mast cell destruction (E. F. Chernushenko, 1978). The presence of skin-sensitizing antibodies was detected using Ovary's passive cutaneous anaphylaxis test (Z. Ovary, 1952). Other tests included the positive intracutaneous allergy test, reproduction of anaphylactic shock event, antigen-specific rosetting and antigen-specific leukocyte fixation (S.M. Pogorelskaya, 1986), moreover, passive allergy transmission was assessed by means of leukocyte mass (C. Prausnitz, 1962) and blood histamine count (G.V. Selyuzhitsky, 1983). Neutrophil functions were analyzed by phagocyte number, phagocyte index, blood phagocytic activity, and metabolic activity with melamine-formaldehyde latex in a spontaneous and latex-stimulated HCT-test (R.V. Petrov, 1989). Lymphokine production was monitored by leukocyte fixation triggered by mitogens such as concanavalin and phytohemagglutinin (S.M. Pogorelskaya, 1986). Antigens produced in the Russian Mycological Center (St. Petersburg) were used in the reactions to determine specific immune responses. An integrated approach was applied to the experimental studies, which allowed analysis homeostasis changes using the principle "dose–organism status" and determining a common parameter for each animal group (V. V. Sadovskiy, 1996). Statistical data analysis was performed using Statistica 6.0 software for Windows (license № AXXR004E642326FA). Differences among study and control groups were analyzed using Student's test. If comparison samples were not normally distributed (according to the Kolmogorov-Smirnov criterion), the non-parametric Mann-Whitney U test was used.

Result and Discussion

The experimental model allowed evaluation of the guinea pig's response to combined exposure to sulfur dioxide and AD [L. M. Sosedova, 2003; L. M. Sosedova, 2010]. This exposure can induce responses that vary with the sequence of administration or intensity of

exposure (Figure 1).

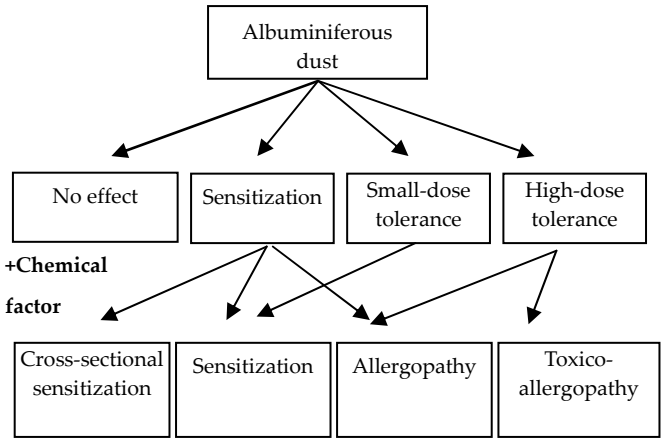

FIG.1 TYPES OF ORGANISM RESPONSE OF GUINEA PIGS TO JOINT EFFECT OF ALBUMINIFEROUS DUST AND CHEMICAL FACTOR

The experimental findings showed sensitization in half of the animals exposed to both AD and sulfur dioxide. Moreover, the intensity of the sensitization was 50%-higher in some animals compared with those that were only exposed to AD. Allergopathy and toxico-allergopathy was found in 25% of the animals in each group. It was possible that the final response depended on the phenotype of the immunoallergologic reaction to allergens. Considering primary sensitization, SDT and HDT, the following effects on health were determined:

- Sulfur dioxide inhalation led to development of allergopathy in animals sensitized to AD. Inhalation simultaneously with or prior to sensitization to AD had insignificant effect on the intensity of the response.
- Sulfur dioxide inhalation made the animals lose their small-dose immunological tolerance, which caused them to become sensitized to AD.
- Sulfur dioxide inhalation with or post HDT resulted in a toxic-allergopathic effect.

Thus, prior inhalation of sulfur dioxide did not lead to HDT but caused apparent allergopathy in experimental animals. The results of experimental modeling of the combined effects of albuminiferous dust (a by-product of biotechnology) and sulfur dioxide (a chemical) made the following conclusions:

- -A response to the combined effects of biological and chemical factors determined by its baseline prenosological conditions may be diverse:
- - The sequence of exposure to biological and chemical factors was important in understanding an animal's quantitative and qualitative response to exposure;
- - It was important to consider both specific and non-specific characteristics of a physiological system functioning taking into account the key role of immune status changes [L. M. Sosedova, 2003; L. M. Sosedova,2010]

Hygienic modeling allowed development of a method to study the combined effects of biological and chemical factors (L. M. Sosedova, 2010) and yielded several significant principles.

- The three baseline models (sensitization, SDT, and HDT) should be created for an experimental study of biological factor exposure of any nature.
- Chemical exposure should occur in the following sequence: prior to, simultaneously with, and post AD injection to determine the most detrimental sequence of administration.
- To understand the feature of the response and evaluation of an animal's condition, and analyze homeostasis changes, it was important to employ the principle "dose–organism status" to evaluate all effects as a whole.

Increases residential were modern production technologies used in the plants located in or near the residential area and the methodological principles outlined here may become the basis for bio-modeling to study the combined effects of different biological and chemical factors.

These experimental studies may allow identification of the cause of the increase in patient complaints of bronchospasmodic syndrome at emergency departments in October 1988 in Angarsk citv [L. M. Sosedova,2003; L. M. Sosedova,2010]. The operation of the biotechnological plant released large amounts of AD into the air of the residential area. AD exposure over several years might cause a prenosological response different depending on immunoallergological phenotype and the quantity of absorbed allergen in sensitive populations. Some people developed latent sensitization to AD; while others developed SDT or HDT; i.e. the organism as a system adapted with a high degree of self-regulation using additional resources reformed to the new level of compensatory adaptation [L. M. Sosedova, 2003; G.M. Bodienkova, 1996].

A prenosological response to AD, and subsequent exposure to a chemical factor led to various types of bronchospasms with allergic or toxic components. Various types of responses might be responsible for different conditions in people, thus physicians registered bronchospasms of both an allergic and a toxic nature.

Thus, the causal or primary factor that prepared an animal to develop bronchospasm was AD, a by-product of a microbial synthesis, and the modified trigger or risk factor was a chemical. Epidemiological, hygienic, and allergological studies suggested sulfurous anhydride which might have been the chemical pollutant which could cause bronchospasm by itself due to its irritating [C. A. Frenga, 1999; F. Riedel, 1988]. Chemical factor exposure to a body with modified specific reactivity to AD can cause recurrent bronchospasmodic allergic or toxic-allergic reactions even when AD was absent in the air. In February 1995, a similar event occurred in Angarsk city, although the biotechnological plant was not in operation at that time. The larger the population that develops sensitization or HDT to AD was, the greater the possibility of a widespread event was. Clinical pathologies can be influenced by contact of an organism with other albuminiferous allergens and the increasing kinds of pollutants in both industrial and agricultural areas (pollen, hair, down, medicine, food, etc.) may have antigenic determinants in common with proteins of biotechnological synthesis.

Extrapolation of the results of experimental studies on humans allowed us to suggest about the nature and causes of the formation of the population of Angarsk bronchospasm. Analysis of experiments on animals showed the development of several forms of response when exposed to AD and sulfur dioxide: sensitization, allergopathy and toxico-allergopathy. Similar symptoms of bronchospasm detected and affected patients.

The lack of monitoring of total biological air pollution including the areas with biotechnological plants didn't allow prediction or evaluation of unfavorable events associated with mass cases of acute toxic-allergic disorders. It should be considered unreasonable to place biotechnological plants in industrial cities or downwind of chemical plants, since it was risky to the population of the combined effects of biological and chemical factors. Moreover, ultraviolet and radiation exposure may cause creation of new compounds with unexpected qualities.

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